DETAILED ACTION

1. Applicant's amendment filed on 07/30/2009 is acknowledged.

2. Claims 1, 4, 15 and 18 are pending and currently under examination as they read on a polypeptide of SEQ ID NO:1 and a kit thereof.

3. In view of the amendment filed on 07/30/2009, only the following rejections are maintained.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 15 stands rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: an allergen consisting of SEQ ID NO:1; a polypeptide consisting of amino acids 181 to 396 of SEQ ID NO:1 and a polypeptide consisting of amino acids 21 to 180 of SEQ ID NO:1, and a composition comprising the allergen and a kit thereof, does not provide reasonable enablement for: a **pharmaceutical composition** comprising an isolated allergen consisting of a polypeptide capable of binding to IgE antibodies from an individual being allergic against mugwort pollen, wherein said polypeptide is selected from the group consisting of : (a) a polypeptide consisting of the amino acid sequence of SEQ ID NO: 1; (b) a polypeptide consisting of the amino acid sequence extending between residues 21 and 180 of SEQ ID NO:1; and (c) a polypeptide consisting of the amino acid extending between residues 181 and 396 of

SEQ ID NO:1 of claim 15. The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation for the same reasons as set forth in the Office Action mailed on 10/06/2008.

Applicant's argument filed on 07/30/2009 has been fully considered, but is not found persuasive.

Applicant argues:

> "Applicants respectfully disagree with the Examiner's position for reasons of record. Nevertheless, in an effort to expedite prosecution, Applicants have amended the claims to be commensurate with the admitted scope of enablement and written description (i.e., replaced "comprising" with "consisting". Accordingly, Applicants respectfully petition for the reconsideration and withdrawal of the outstanding rejections under 35 U.S.C. § 112, first paragraph."

The specification and 1.132 declaration filed by Fatima Ferreira on 07/25/2008 are not sufficient to support the recitation of a pharmaceutical composition in claim 15. The in vitro T cell response data in Appendix A is not commensurate in scope with the claimed pharmaceutical composition. The Examiner finds no in vivo data in the specification, declaration or post-dated art to support the contention that the claims allergen can be used as in a pharmaceutical composition, nor are any in vitro experiments disclosed that reasonably correlate with in vivo effectiveness. In view of the absence of a specific and detailed description in Applicant's specification of how to effectively use the pharmaceutical composition as claimed, absence of working examples providing evidence which is reasonably predictive that the claimed pharmaceutical compositions are effective for in vivo use, and the lack of predictability in the art at the time the invention was made, an undue amount of experimentation would be required to practice the claimed pharmaceutical composition with a reasonable expectation of success.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Applicant's general arguments with respect to all of the following rejections under 102(b) and 103 have been fully considered, but are not found persuasive.

Applicant argues:

> "For reasons of record, Applicants continue to reject the Examiner's suggestion that the burden is on Applicants to show that the presently claimed allergen (SEQ ID NO: 1) is not identical to any of the allergens of the cited prior art or *vice versa*. In the previous office action, Examiner admits that "[n]o sequence information is provided to unequivocably prove that any of the isolated polypeptides is indeed identical to At v 6 [sic]". However, she is satisfied with the fact that none of the information provided unequivocably proves that the isolated proteins of the prior art are not the recited Art v 6 of SEQ ID NO: 1. Applicants respectfully submit that the Examiner has a fundamental misunderstanding of the doctrine of inherency and the respective burdens arising therefrom.
>
> Under the principle of inherency, **anticipation may not be established by probabilities or possibilities** ("A prior art event cannot be established based on speculation, or where a doubt exists." *Ethyl Molded Product Co. v. Betts Package, Inc.*, 9 USPQ 2d 1001, 1032-33 (E.D.KY 1988). Rather, the doctrine of inherency is available only when the prior inherent event can be established with **certainty.** The Court of Appeals for the Federal Circuit ("CAFC") closely follows this doctrine, finding inherent anticipation only when an alleged inherent fact is **"necessarily present"** in the prior art, and not merely sometimes, occasionally, or possibly present.[2] Thus, for a claimed product to be characterized as inherently disclosed, it must be a **"natural result flowing from the operation as taught"** in the prior art. *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331, 1343 (Fed. Cir. 2005). Importantly, when relying upon the theory of inherency, it is the Examiner's burden to provide facts or reasoning that reasonably support the determination that the allegedly inherent characteristic **necessarily** flows from the teachings of the applied prior art. *Exparte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990). In other words, the evidence must make clear that the missing descriptive matter is **necessarily present** in the thing described in the reference. Inherency, however, may not be established by probabilities or possibilities. Accordingly, the "mere fact that a certain thing **may result** from a given set of circumstances **is not sufficient".** *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999), emphasis added. Likewise, the

suggestion that **a** certain result or characteristic **may occur** or be present in the prior art **is not sufficient** to establish the inherency of that result or characteristic. *In re Rijckaert,* 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993); see also *In re Oelrich,* 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). In sum, inherency must be a necessary result and not merely a possibility.

Thus, contrary to the Examiner's suggestion, the burden of "unequivocable proof" lies not with Applicants but with the Examiner, who must prove that the claimed invention is a "necessary and inevitable" consequence of the disclosure in a prior art reference. See Schering Corp. v. Geneva Pharmaceuticals, Inc., 339 F. 3d 1373, 1375 (Fed. Cir. 2003). As discussed previously and herein below, not only is Applicants' claimed mugwort pollen allergen "Art v 6" of SEQ ID NO: 1 not certainly, necessarily, and inevitably present in the prior art disclosures but, given the ample rebuttal of record, substantial doubt exists as to its presence at all. While the Examiner repeatedly states that the approximately 44 kDa protein of the prior art is the claimed allergen "absent evidence to the contrary", Applicants respectfully submit that prosecution history is replete with "evidence to the contrary", facts, data, and expert opinion that substantially undermine the Examiner's suggestion that the various prior art protein bands extracted from mugwort pollen are identical to and therefore inherently anticipate Applicants' claims to the allergen of SEQ ID NO: 1.

Nevertheless, in an attempt to conclusively demonstrate that the claimed allergen peptide is not "necessarily present" in the prior art disclosures, Applicant submitted comparative data that raised significant doubts as to the validity of the Examiner's unwavering yet unsubstantiated assertions of inherent anticipation. In particular, Applicants submitted a listing of several potentially allergenic proteins having molecular weights ranging of 40 to 44kDa found to coexist in mugwort pollen extract (See Appendix B to the July 25th declaration of Dr. Ferreira). Setting aside Art v 6 (SEQ ID NO: 1) of the present invention, four of the eight proteins isolated from the 40-44kDa band of the mugwort pollen extract and described in Appendix B are known to possess allergenic activity. In particular: • Phosphoglycercate kinase (Calculated MW of 42.3) has been identified as an allergen in the fungus Epicoccoum purpurascens (Kukreja et al., 2008); • Enolase (Calculated MW of 47.8) has been identified as an allergen in latex as well as in several fungi (Cladosporium, Alternaria) as well as yeast (Posch et al., 1997); •Fructose bisphosphate aldolase (Calculated MW of 38.4) has been identified as a known food allergen found in wheat flour (Baur et al., 1998); and Malate dehydrogenase (Calculated MW of 35.5) has been identified as an allergen in the yeast Malasseziafurfur (Onishi et al., 1999).

Accordingly, the "approximately 44 kDa" proteins identified in the cited prior art references are just as likely be one of these four known allergen proteins as they are to be Applicants' SEQ ID NO: 1. Thus, Applicants respectfully submit that the requisite certainty is noticeably absent from the instant case of inherent anticipation.

The Examiner dismissed the previously evidence on the grounds that there was no showing that these proteins are recognized by IgE or serum of mugwort-pollen allergic patients as described in the prior art, summarily disregarding Dr. Ferreira's expert opinion that "it can be presumed with high certainty that these 4 enzymes are also allergens in mugwort due to their high evolutionary sequence conservation." (See point 9 of the July 25, 2009 declaration of Dr. Fatima Ferreira). However, the degree to which a single allergen may cross-react with allergens from other species, even other families, is borne out by Applicants' Exhibit One, an article by Patricia Barral, et al. (J. Immunol., 2004, 172:3644-3651), a copy of which is provided herewith. Barral et al. demonstrate that an allergen from olive tree pollen, Ole e 10, shares IgE B cell epitopes with proteins from other allergen sources, including Oleaceae, Gramineae, Betulaceae, Chenopodiaceae, Cupressaceae, Ambrosia, and Parietaria pollens, latex, and vegetable foods, such as tomato, kiwi, potato, and peach, indicating that Ole e 10 is a pan- allergenic plant protein that shows notable intra- and interspecie IgE cross reactivity. Applicants also direct the Examiner's attention to their Exhibit Two, an article by Rosa Sanchez-Monge, et al. ("Chapter 6: Can cross-reactivity studies enable generic allergy prevention", Allergy Matters, Ed. Ludd et al., Vol. 10, March 2005), the first line of which reads "The occurrence of homologous proteins in foods, pollen and latex is the molecular basis of the plant

> sources' allergenic cross-reactivity." Thus, one would reasonably expect, at a minimum, that a known latex allergen (i.e., enolase) and a known food allergen (i.e., wheat flour allergen fructose bisophosphate aldolase) would cross-react with IgE from other allergen sources, such as IgE or serum of mugwort-pollen allergic patients, particularly when such allergens are isolated from a mugwort pollen extract. Accordingly, Applicants reiterate that the various "approximately 44 kDa" proteins described by the prior art have only a one in five chance of being Applicants' SEQ ID NO: 1. Again, since the requisite certainty is noticeably absent, the prior art disclosures cannot be fairly characterized as inherently anticipating the invention of the pending claims.

It remains the Examiner's position that all of the prior art references performed the same methods that were performed in the instant application to arrive at instant SEQ ID NO:1. Namely, *Artemisia vulgaris* pollen extract was run on a gel to separate the individual proteins present in the sample. The gel was then probed with serum from individuals known to be *A. vulgaris* allergic. IgE binding of particular proteins was demonstrated, among which was a protein of approximately 44 kDa in each prior art reference. In addition to the fact that is Applicant's burden to show that the reference allergen is not the allergen recited in the claim, there is no reason to believe that the instant protein of SEQ ID NO:1 which is present in *A. vulgaris* pollen was not isolated by a method that isolated all of the proteins present in *A. vulgaris* pollen and which showed that particular proteins that were isolated reacted with IgE from *A. vulgaris* allergic patients. "It is well settled that a prior art reference may anticipate when the claim limitations not expressly found in that reference are nonetheless inherent in it." *In re Cruciferous Sprout Litigation,* 301 F.3d 1343, 1349 (Fed. Cir. 2002). See, e.g., *MEHL/Biophile Int'l Corp. v. Milgraum,* 192 F.3d 1362, 1365 (Fed.Cir.1999) ("Under the principles of inherency, if the prior art necessarily functions in accordance with, or includes, the claimed limitations, it anticipates.")

Applicant's argument that there are proteins that are present in *A. vulgaris* pollen that are of approximately the same molecular weight as instant SEQ ID NO:1; and therefore such a fact casts doubt on the presence of the protein of SEQ ID NO:1 being isolated in a band on the gels in the prior art is not persuasive. If those proteins which Applicant claims are present would be present on the gel, then so would SEQ ID NO:1. In addition, it remains the Examiner's position that the list of 2 40-44 kDa proteins found in *A. vulgaris* pollen other than instant SEQ ID NO:1, only one of which has been demonstrated to be an allergen in fungus provided in Appendix B in the declaration filed on 07/25/2008 is not persuasive to show that the reference proteins are not SEQ ID NO:1. The proteins listed in Appendix B were not shown to bind IgE from *A. vulgaris* pollen allergic individuals, as required by the claims and as demonstrated in the prior art. If Applicant is trying to say that the prior art bands are those proteins they must at a minimum demonstrate that they actually bind *A. vulgaris* allergic patient IgE, like the reference proteins do and like SEQ ID NO:1 does. Because one protein of 40-44 kDa found in fungus was found to bind IgE does not mean that it is a major or minor allergen that will bind IgE from patients allergic to *A. vulgaris* pollen. Applicant's arguments with regard to cross-reactivity are unpersuasive as well. First, it is noted that no references were submitted with this response as Applicant said *supra.* Second, Applicant has not shown that cross-reactivity can be demonstrated with regard to any of the particular proteins and enzymes listed in Appendix B.

7. Claims 1 and 4 stand rejected under 35 U.S.C. 102(b) as being anticipated by Nilsen et al. (of record) as evidenced by http://www.allergen.org/allergen.aspx (of record) and GenBank

Accession Number AY904433 (of record) for the same reasons as set forth in the Office Action mailed on 10/06/2008.

Applicant's arguments filed on 07/30/2009 have been fully considered, but are not found persuasive.

Applicant argues

> "With regard to Nilsen, the Examiner specifically points to the "approximately 44 kDa" (actually - 43 kDa) bands found in lanes C, E, F, and K of Figure 1, as well as the disclosures in Table 1. However, of the proteins that might be characterized having a molecular weight of approximately 40.9 kDa (i.e., those having MW of 34, 39, 42, and 48 kDa), two showed no virtually no reactivity with IgE from mugwort patient serum (MW 34, 48 kDa). Although the remaining two bound IgE from 94% of the patients tested, they demonstrated only weak to medium radio-staining (MW 39 and 42 kDa), which suggests either a weak affinity for mugwort patient IgE and/or a lack of specific binding to mugwort patient IgE. In contrast, Applicants' Art v 6 of SEQ ID NO: 1 (MW 40.9 kDa) has been shown to be significantly less common in the population, binding only 36%[3] to 49.4%[4] of mugwort patient IgE. Given the divergence in prevalence, there is no reason to believe that either of Nilsen's doublet band proteins (i.e., the 39,000 or the 42,000 kDa protein) is identical to Applicants' SEQ ID NO: 1."

Applicant has not met their burden to show that the allergen in Nilsen et al. is not the allergen of SEQ ID NO:1 by saying that only 36-49 percent of *A. vulgaris* allergic patients have IgE that binds to instant Art v 6 of SEQ ID NO:1. The divergence in prevalence of binding is not sufficient to prove that the reference protein is not the protein of SEQ ID NO:1 because IgE reactivity of different allergens in *A. vulgaris* pollen depends on individual reactivity. The particular patient sample in Nilsen et al. could very likely have different reactivity than the general patient population. This does not mean that the reference protein is not SEQ ID NO:1. *Artemisia vulgaris* pollen was isolated and the extracts were probed with *A. vulgaris* pollen allergic individuals. There is no reason to think that the band that was isolated in Nilsen is not the protein of SEQ ID NO:1 since the protein was isolated in the exact same manner in the

instant invention. Therefore, it remains the Examiner's position that the reference protein is the protein of SEQ ID NO:1 because it is an allergen that binds to IgE from allergic patients and it has been isolated from *A. vulgaris* pollen, just like the protein of SEQ ID NO:1. Since the office does not have a laboratory to test the reference allergen, it is applicant's burden to show that the reference allergen is not the allergen recited in the claim. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

8. Claims 1 and 4 stand rejected under 35 U.S.C. 102(b) as being anticipated by Brandys et al. (of record) as evidenced by http://www.allergen.org/allergen.aspx (of record) and GenBank Accession Number AY904433 (of record) for the same reasons as set forth in the Office Action mailed on 10/06/2008.

Applicant's arguments filed on 07/30/2009 have been fully considered, but are not found persuasive.

Applicant argues

> "With regard to Brandys, the Examiner points to the "approximately 44 kDa" (actually ~43 kDa) bands found in lanes v, c, s, and p of Figure 2C. However, Applicants wish to point out that only lane "v" corresponds to mugwort pollen *(Artemisia vulgaris);* lanes c, s, and p correspond to other Artemisia species *(A. campestris, A. scoparia,* and *A. princeps)* and are therefore irrelevant to the present inquiry. In any event, like Nilsen, Brandys observed that the 40-42 MW extract isolated from mugwort pollen extract bound a "significant majority" of mugwort patient IgE (8 of 10), though with weak affinity (see Table 2). As noted above, Applicants' Art v 6 of SEQ ID NO: 1 (MW 40.9 kDa) is less significantly common, binding only 36% to 49.4% of mugwort patient IgE. Furthermore, Brandys observed the IgE component(s) found in *Artemisia vulgaris* to have a pI on the order of 4.55 (see Figure 3B), which is completely inopposite to Applicants' SEQ ID NO: 1 with a pI of 8.27. Given these critical distinctions, there is no reason to believe that the 43 kDa mugwort pollen extract protein identified by Brandys is identical to Applicants' SEQ ID NO: 1."

Applicant has not met their burden to show that the allergen in Brandys et al. is not the allergen of SEQ ID NO:1 by saying that only 36-49 percent of *A. vulgaris* allergic patients have IgE that binds to instant Art v 6 of SEQ ID NO:1. The divergence in prevalence of binding is not sufficient to prove that the reference protein is not the protein of SEQ ID NO:1 because IgE reactivity of different allergens in *A. vulgaris* pollen depends on individual reactivity. The particular patient sample in Brandys et al. could very likely have different reactivity than the general patient population. This does not mean that the reference protein is not SEQ ID NO:1. *Artemisia vulgaris* pollen was isolated and the extracts were probed with *A. vulgaris* pollen allergic individuals. There is no reason to think that the band that was isolated in Brandys is not the protein of SEQ ID NO:1 since the protein was isolated in the exact same manner in the instant invention. Applicant's argument that the pI of the reference protein is inopposite to the protein of SEQ ID NO:1 as demonstrated in Figure 3B is not persuasive. As one can readily discern in Figure 2C, there is more than one IgE binding protein in lane v. All of those proteins would have to have the same pI if one looks at Figure 3B. However, that is very unlikely. Applicant is directed to Figure 7A which shows in lanes 1-9 that Norweigen patients possess different IgE binding profiles for the A. vulgaris allergens. As one can readily discern, *A. vulgaris* pollen comprises a number of different *A. vulgaris* allergic IgE binding proteins with many different pIs. In particular, attention is called to lanes 8 and 9, which have bands in the range of the pI of SEQ ID NO:1. Attention is also called to Table 2, which shows that A. vulgaris has 5 separate IgE binding components, one of which is specifically a 40-42 kDa component. Therefore, it remains the Examiner's position that the reference protein is the protein

of SEQ ID NO:1 because it is an allergen that binds to IgE from allergic patients and it has been isolated from *A. vulgaris* pollen, just like the protein of SEQ ID NO:1. Since the office does not have a laboratory to test the reference allergen, it is applicant's burden to show that the reference allergen is not the allergen recited in the claim. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980). Applicant's argument is not sufficient to overcome the rejection.

9. Claims 1 and 4 stand rejected under 35 U.S.C. 102(b) as being anticipated by Hirschwehr et al. (of record) as evidenced by http://www.allergen.org/allergen.aspx (of record) and GenBank Accession Number AY904433 (of record) for the same reasons as set forth in the Office Action mailed on 10/06/2008.

Applicant's arguments filed on 07/30/2009 have been fully considered, but are not found persuasive.

Applicant argues

> "With regard to Hirschwehr, the Examiner points to the "approximately 44 kDa" (actually ~46 kDa) bands found in lanes 10, 11, and 13 of Figure 1A and lanes 6 and 7 of Figure 3A, and patients A & B of Figure 5, patients A & B. However, like Nilsen and Brandys,Hirschwehr characterized the 46kDa fraction as a "prominent IgE-binding band" detected in mugwort pollen extract "by most of the sera". See p. 199, col. 2 at bottom. In contrast, Applicants' Art v 6 of SEQ ID NO: 1 (MW 40.9 kDa) is less significantly prevalent in the population, binding only 36% to 49.4% ofmugwort allergic patient IgE. Thus, there is no reason to believe that the 46 kDa mugwort pollen extract protein identified by Brandys is identical to Applicants' SEQ ID NO: 1."

Applicant has not met their burden to show that the allergen in Hirschwehr et al. is not the allergen of SEQ ID NO:1 by saying that only 36-49 percent of *A. vulgaris* allergic patients have IgE that binds to instant Art v 6 of SEQ ID NO:1. The divergence in prevalence of binding is not sufficient to prove that the reference protein is not the protein of SEQ ID NO:1 because IgE reactivity of different allergens in *A. vulgaris* pollen depends on individual reactivity. The particular patient sample in Hirschwehr et al. could very likely have different reactivity than the general patient population. This does not mean that the reference protein is not SEQ ID NO:1. *Artemisia vulgaris* pollen was isolated and the extracts were probed with *A. vulgaris* pollen allergic individuals. There is no reason to think that the band that was isolated in Hirschwehr is not the protein of SEQ ID NO:1 since the protein was isolated in the exact same manner in the instant invention. Therefore, it remains the Examiner's position that the reference protein is the protein of SEQ ID NO:1 because it is an allergen that binds to IgE from allergic patients and it has been isolated from *A. vulgaris* pollen, just like the protein of SEQ ID NO:1. Since the office does not have a laboratory to test the reference allergen, it is applicant's burden to show that the reference allergen is not the allergen recited in the claim. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

10. Claims 1 and 4 stand rejected under 35 U.S.C. 102(b) as being anticipated by De La Hoz et al. (of record) as evidenced by http://www.allergen.org/allergen.aspx (of record) and GenBank Accession Number AY904433 (of record) for the same reasons as set forth in the Office Action mailed on 10/06/2008.

Applicant's arguments filed on 07/30/2009 have been fully considered, but are not found persuasive.

Applicant argues:

> "With regard to De la Hoz, the Examiner points to the "approximately 44 kDa" (actually ~42.7 kDa) bands found in lanes A and B of Figure 3 and lanes A, B, and C Figure 4. Like Nilsen, Brandys, and Hirschwehr, De la Hoz observed that the approximately 42.7 kDa mugwort protein, incorrectly dubbed "Art v 1", bound IgE from 68% of the patients tested (see Table 2). As noted above, Applicants' Art v 6 of SEQ ID NO: 1 (MW 40.9 kDa) is less significantly prevalent in the population, binding only 36% to 49.4% of mugwort allergic patient IgE. In addition, the De la Hoz "Art v 1" protein is an acidic protein with a pI of 4.4 and a denaturing (SDS-PAGE) molecular weight of approximately 60 kDa whereas Applicants' "Art v 6" protein is a basic protein with a pI of 8.27 and a denaturing (SDS-PAGE) molecular weight of approximately 40 kDa. Contrary to the Examiner's suggestion, these completely inopposite parameters are not merely experimental "discrepancies" but conclusive proof that the "Art v 1" mugwort pollen extract protein identified by De la Hoz is not the "Art v 6" protein of SEQ ID NO: 1. "

It is the Examiner's position that De La Hoz does not only teach the incorrectly dubbed 'Art v 1' protein. It teaches the isolation of all IgE binding proteins found in *A. vulgaris* pollen, particularly one whose band is below the 42.7 kDa. The reference does not teach that this band has a pI of 4.4. The reference teaches that the 47kDa band has a pI of 4.4. As one can readily ascertain in Figure 5, there is a protein that binds *A. vulgaris* pollen allergic IgE with a pI in the range of 8.27. This fact is further taught in De la Hoz on page 651, third full paragraph.

Applicant has not met their burden to show that the allergen in De La Hoz et al. is not the allergen of SEQ ID NO:1 by saying that only 36-49 percent of *A. vulgaris* allergic patients have IgE that binds to instant Art v 6 of SEQ ID NO:1. The divergence in prevalence of binding is not sufficient to prove that the reference protein is not the protein of SEQ ID NO:1 because IgE reactivity of different allergens in *A. vulgaris* pollen depends on individual reactivity. The particular patient sample in De La Hoz et al. could very likely have different reactivity than the

general patient population. This does not mean that the reference protein is not SEQ ID NO:1. *A. vulgaris* pollen was isolated and the extracts were probed with *A. vulgaris* pollen allergic individuals. There is no reason to think that the band that was isolated in De La Hoz is not the protein of SEQ ID NO:1 since the protein was isolated in the exact same manner in the instant invention. Therefore, it remains the Examiner's position that the reference protein is the protein of SEQ ID NO:1 because it is an allergen that binds to IgE from allergic patients and it has been isolated from *A. vulgaris* pollen, just like the protein of SEQ ID NO:1. Since the office does not have a laboratory to test the reference allergen, it is applicant's burden to show that the reference allergen is not the allergen recited in the claim. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nilsen et al. (of record), Brandys et al. (of record), Hirschwehr et al. (of record), De La Hoz et al. (of record), each as evidenced by http://www.allergen.org/allergen.aspx (of record) and GenBank Accession

Number AY904433 (of record) each in view of U.S. Patent 4,459,360 (of record) for the same reasons as set forth in the Office Action mailed on 10/06/2008.

Applicant's arguments filed on 07/30/2009 have been fully considered, but are not found persuasive.

> Applicant argues that US '360 fails to cure the above-noted deficiencies of the Nilsen et al., Brandys et al., Hirschwehr et al. and De La Hoz et al. references, namely the disclosure of an allergen consisting of SEQ ID NO: 1 that binds mugwort patient IgE antibodies. Thus, in that the prior art references, alone or in combination, fail to teach or suggest all the claim limitations, Applicants respectfully submit that the Examiner has failed to set forth a *prima facie* case of obviousness. Accordingly, Applicants respectfully request reconsideration and withdrawal of the obviousness rejection of claim 18 in view of the amendments and remarks herein.

It remains the Examiner's position that Nilsen et al., Brandys et al., Hirschwehr et al. and De La Hoz et al. teach the protein of SEQ ID NO:1 for the reasons set forth in the Office Action mailed on 10/06/2008 and *supra*. It also remains the Examiner's position that it would have been obvious to one of ordinary skill in the art at the time of invention to use the isolated allergen band of Nilsen et al., Brandys et al., Hirschwehr et al., or De La Hoz et al. in a diagnostic kit for allergy screening for that allergen as taught by the '360 Patent because the '360 Patent teaches that such a kit would be economical, easy to analyze and useful as an allergy screening system.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

October 21, 2009
Nora M. Rooney
Patent Examiner
Technology Center 1600

/Maher M. Haddad/
Primary Examiner,
Art Unit 1644